SPECIAL ISSUE

Special Issue - 'Frontiers of Simulation and Experimentation for Personalised Cardiovascular Management and Treatment'

EDITORIAL

Cardiovascular diseases (CVDs) are the number 1 cause of death globally, taking an estimated 17.9 million lives each year. CVDs are a group of disorders of the heart and blood vessels and include coronary heart disease, cerebrovascular disease, rheumatic heart disease and other conditions. One third of these deaths occur prematurely in people under 70 years of age.

Tackling cardiovascular disease requires synergistic and innovative approaches between a number of disciplines -including engineering- to develop and use technologies to understand the biological mechanisms of CVD and the consequences of personalised surgical interventions, and also, to design and assess devices under physiological or pathological conditions.

This special issue comprises a collection of selected papers from the conference 'Frontiers of Simulation and Experimentation for Personalised Cardiovascular Management and Treatment'.

The two day Conference was held at University College London, as part of the dissemination programme of the ITN European Training Network VPH-Cardiovascular Simulation and Experimentation for Personalised Medical Devices, focusing on state-of-the-art developments in personalised cardiovascular support, underpinned by simulation and experimentation and building on the foundations of the Virtual Physiological Human (VPH) Initiative.

The event was organised by Prof Vanessa Diaz with the support of UCL Engineering, UCL Mechanical Engineering, UCL Institute of Healthcare Engineering, Wellcome/EPSRC Centre for Interventional and Surgical Sciences (WEISS), Leeds Test Objects, Insigneo, Ansys and CERTARA. It provided a forum for early career researchers to showcase their work on cardiovascular engineering for personalised interventions and to network and exchange ideas with experienced researchers, engineers, industry and clinicians. The quality of presentations was excellent providing a testament of the talent that the field attracts.

The quest to develop patient specific in silico tools to understand haemodynamics and personalise the management of cardiovascular diseases by fusing medical images with CFD tools continues to be a strong driver in the field. The contributors in this special issue have demonstrated superb skill in developing workflows that enable patient specific modelling using available imaging modalities and routinely used clinical data and addressing the impact of boundary conditions and approximations on the accuracy of the CFD simulations.

Biffi et al. presented a semi-automatic workflow for patient specific modelling of mitral valve regurgitation. By combining multiple image modalities (CMR, 3D TOE), FSI numerical methods based on FE and SPH methods, they successfully reproduced the patient specific flow and mechanics of the pathological MV, opening opportunities for the personalised treatment of MV diseases and in silico testing of devices.

The fusion of medical images and simulations was also demonstrated on two complex pathologies of the aorta: aortic dissection and coarctation. Bonfanti et al. engineered a computational framework to simulate the haemodynamics in patient specific cases of Type B dissected aortas with complex anatomies and multiple tears, using data routinely used in the clinic to monitor patients, namely CT scans and Doppler ultrasound. Dynamic boundary conditions were used at the outlets tuned through an optimisation procedure. The aortic

compliance was modelled using a capacitor improving the realism of simulation based on the rigid wall approximation and avoiding computationally demanding FSI procedures. The simulations were validated against invasive pressure measurements and provided insight on the influence of the tears on the distribution of pressure and wall shear stress markers, highlighting the prognostic value of simulation based hemodynamic indices.

A similar approach was adopted by Mercuri et al. for the study of aortic coarctations. The authors developed a 3D/0D multiscale modelling approach to study the hemodynamics of 11 patients assessed before and after coarctation repair. They built their pipeline using MR data (CE-MRA and 2D cine MR) and cuff pressure measurements. A 1D/0D approach was used to tune the outflow boundary conditions in an automatic fashion. The study allowed aortic distensibility to be included through the 2D-PC MRI flow waves without the need of FSI studies offering an advantage over previous studies on coarctation where such effects were neglected.

Identifying ulcerated coronary plaques is a challenge for clinicians. Migliori et al. demonstrated that an OCT based reconstruction algorithm coupled with CFD simulations of pre- and post operative haemodynamics can address this challenge, revealing both the disrupted flow patterns of the ulcerated plaque and the flow recovery following stenting. The framework highlights the importance of haemodynamic studies in the management of coronary disease.

Coronary disease was also the topic of the study presented by Lo et al. They tackled the challenges of accurate fractional flow reserve (FFR) computations for the evaluation of the severity of coronary artery stenosis by integrating Computed Tomography Coronary Angiography (CTCA) and Positron Emission Tomography (PET) perfusion imaging into CT-based FFR measurements. They explored the impact of outflow boundary conditions on 3D patient specific simulations, showing that perfusion data although not routinely acquired can provide a more accurate representation of vasodilatory response

Why some peripheral grafts heal and why some peripheral grafts fail due to neointimal hyperplasia (NIH) growth remains an open question in vascular Surgery. Many have hypothesised that a compliance mismatch between the native artery and the grafted vein is a key driver for the development of NIH. Donadoni et al., used a combined methodology (computational fluid dynamics & NIH evolution model) to assess the impact of compliance mismatch on three patient-specific peripheral bypass grafts in two different post-operative scenario: compliant arterial segments and rigid venous graft and compliant arteriovenous graft. In both cases, the presence of quasi-rigid surgical stitches was accounted for and results show that compliance mismatch seems to have a small effect in haemodynamic indices linked to NIH growth, indicating that the search for plausible mechanisms for graft failure continues.

Acute ischaemic stroke is caused by thrombosis or embolism that occludes a cerebral vessel supplying a specific area of the brain. Gu et al. simulated thrombolytic therapy in ischaemic stroke in patient-specific cases. They successfully showed *in silico* that clot size has a strong influence on recanalisation success and lysis time, which could potentially pave the way to help clinicians understand if a patient is more likely to achieve successful recanalisation with intravenous thrombolysis within a limited time window.

Vessel compliance remains one of the challenges in in silico models of cardiovascular disease, partly because tissue properties are difficult to determine for FSI studies. In this special issue an in vivo estimation of myocardial contractility is presented by Rumindo et al. based on non-invasive routine cardiac MR data and inverse finite element modelling of the left ventricle. Subject specific LV biomechanical indices extracted from 21 healthy patient datasets and validated against published values indicated the prognostic potential of the method for myocardial disease.

In vitro tools to estimate cardiac deformation were also demonstrated by Ferraiuoli et al. Using a porcine heart, 3D digital image correlation (3D-DIC) and ultrasound 2D speckle-tracking echocardiography (US-2D-STE) they showed that digital image correlation could provide

dynamic measurements of displacement and strain and potentially be used with ex vivo beating heart platforms to provide insight into the contraction of the heart.

Finally, Gomez-Bardon et al reminded us that CFD modelling of medical devices might be more complex that is thought as the blood constituents are heterogeneously distributed in complex configurations such as those found in blood oxygenators. They produced microfluidic constructs that mimic the fibers of blood oxygenators and perfused them with human blood revealing the non-uniform haematocrit distributions therein and calling for more sophisticated CFD models accounting for the particulate phase of blood.

We would like to thank all the researchers who contributed to this special issue, the reviewers who assessed the submitted work and the Editor for providing us with the opportunity to assemble this collection. In silico and in vitro studies to enable personalised treatment is an active area of research which has the potential to revolutionise the way we treat disease. This Special Issue provides only a snapshot of recent developments in the field, and hopefully can stimulate further research that will translate into clinical outcomes in the not too distant future.

Guest Editors
Vanessa Diaz, Stavroula Balabani
WEISS
Department of Mechanical Engineering
Faculty of Engineering Science
University College London, UK